

## **AMENDMENT ENTRY**

Amendment of 12/10/08 has been entered. Claims 1, 3-22 and 24-28 are pending and are under examination.

The amendment of 12/10/08 has failed to follow 37 CFR 1.121 in the recitation of claim 10, since claim 10 did not recite dependency from claim "1", as in the amendment of 2/20/07. Claim 10 is presented herein below as it should have appeared, with proper markings, in the amendment of 12/10/08.

10. (Currently Amended) The method of claim 1 further comprising treating the flow-through of the first anion-exchange chromatography with solvent detergent for ~~about~~ 4.5 to ~~about~~ 8 hours to inactivate lipid coated viruses.

## **EXAMINER'S AMENDMENT**

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Matthew Kelley on 2/25/09.

A complete listing of the claims, with the changes entered by examiner's amendment, follows.

1. (Currently Amended) A method of preparing a purified, virus inactivated and virus safe antibody preparation from a starting solution comprising antibodies and contaminants, the method comprising the steps of:

(a) adjusting the pH of the starting solution to 4.8 to 4.95, to produce an intermediate solution;

(b) adding caprylate and/or heptanoate ions to the intermediate solution and maintaining the pH at 4.8 to 4.95, whereby a precipitate is formed and the antibodies are essentially present in a supernatant;

(c) incubating the supernatant under conditions of caprylate and/or heptanoate ion concentration, time, pH and temperature to form a second precipitate ~~achieve precipitation of non-IgG proteins~~ and filtering to form a filtered solution;

(d) applying the filtered solution to a first chromatographic column filled with a first anion exchange resin at a pH from about 5.0 to about 5.2 to perform a first anion-exchange chromatography under conditions that allow binding of contaminants to the resin while not allowing significant binding of the antibodies to the resin, wherein a purified, virus inactivated and virus safe antibody preparation is produced as flow-through.

2. (Cancelled)
3. (Previously Presented) The method of claim 1 further comprising performing a second anion exchange chromatography at a pH range of from 6.7 to 6.9.
4. (Previously Presented) The method of claim 1 wherein steps (b) and (c) are repeated at least one time.
5. (Previously Presented) The method of claim 1 wherein the starting solution comprises plasma-derived antibodies.
6. (Currently Amended) The method of claim 1 further comprising applying the flow-through of the first chromatographic column to a second chromatographic column filled with a second anion exchange resin to perform a second anion-exchange chromatography under conditions that allow binding of contaminants to the ~~resins~~ resin while not allowing significant binding of the antibodies to the resins.
7. (Previously Presented) The method of claim 1, wherein the antibodies are immunoglobulin G.

8. (Previously Presented) The method of claim 6, where the pH is adjusted to 6.7 to 6.9 prior to the second anion-exchange chromatography.
9. (Previously Presented) The method of claim 1 further comprising concentrating the anion-exchange chromatography flow-through to 60 to 90 mg/ml and diafiltrating the anion-exchange chromatography flow-through against a buffer solution.
10. (Previously Presented) The method of claim 1 further comprising treating the flow-through of the first anion-exchange chromatography with solvent detergent for 4.5 to 8 hours to inactivate lipid coated viruses.
11. (Previously Presented) The method of claim 10, further comprising removing the detergents of the incubation mixture by solid and liquid phase extraction.
12. (Currently Amended) The method of claim 1 further comprising combining the caprylate ~~treatment~~ incubation with one or more of the following-UV-C treatment, heat-treatment, virus filtration, and prion removal or inactivation.

13. (Previously Presented) The method of claim 11, further comprising adjusting the pH value upon solid phase extraction to 6.7 to 6.9.

14. (Currently Amended) The method of claim 13, further comprising submitting the solution to the second anion-exchange chromatography flow-through of the first chromatographic column to a second chromatographic column filled with a second-anion exchange resin to perform a second anion-exchange chromatography under conditions that allow binding of contaminants to the resin while not allowing significant binding of the antibodies to the resins, wherein a purified, virus inactivated and virus safe antibody preparation is produced as a second-anion exchanger flow-through.

15. (Currently Amended) The method of claim 14, further comprising adjusting the pH value of the second anion-exchanger flow-through to 3.5 to 4.5 to provide a pH-adjusted second anion-exchanger flow-through solution.

16. (Currently Amended) The method of claim 15, wherein the antibodies are IgG and further comprising contacting the IgG pH-adjusted second anion-exchanger flow-through solution by a virus filter.

17. (Currently Amended) The method of claim 15, wherein the antibodies are IgG and further comprising contacting the ~~IgG~~ pH-adjusted second anion-exchanger flow-through solution by a nanofilter.

18. (Currently Amended) The method of claim 15 wherein the antibodies are IgG and further comprising incubating the ~~IgG~~ pH-adjusted second anion-exchanger flow-through solution for at least 24 hours.

19. (Currently Amended) The method of claim 15, wherein the antibodies are IgG and further comprising concentrating the ~~IgG~~ pH-adjusted second anion-exchanger flow-through solution to 5 or 10% (w/v) to form a concentrate.

20. (Previously Presented) The method of claim 19, wherein the osmolality of the concentrate is 200 to 400 mOsmol/kg.

21. (Previously Presented) The method of claim 20, further comprising adjusting the pH of the IgG concentrate to 3.5 to 6.0.

22. (Previously Presented) The method of claim 21 further comprising sterile filtering and filling the IgG concentrate in glass bottles or plastic containers.

23. (Cancelled).

24. (Previously Presented) The method of claim 9 wherein the buffer solution is a phosphate buffer solution.

25. (Previously Presented) The method of claim 10 wherein the solvent detergent is Triton X-100 and TnBP.

26. (Previously Presented) The method of claim 25 wherein the concentration is 1% Triton and 0.3% TnBP.

27. (Currently Amended) The method of claim 15, wherein the pH of the second anion-exchanger flow-through is adjusted to about 4.0 +/- 0.1.

28. (Previously Presented) The method of claim 18, wherein the incubation temperature is  $37^{\circ}\text{C} \pm 1^{\circ}\text{C}$ .

#### EXAMINER'S COMMENT

In claim 1, the change in step c) avoids over limiting what is precipitated by caprylate or heptanoate. For example, page 7, lines 15-16 of the disclosure indicates that there would still be some non-precipitated IgA that needs to be removed by anion exchange. The concluding change in step c) provides antecedent basis for "the filtered solution" in step d). The change in step d) provides antecedent basis for "the first anion exchange chromatography" in claim 10.

In claim 6, the change at line 2 is for mere clarification. The change at line 3 provides antecedent basis for "the second anion-exchange chromatography" in claim 8. The change at line 4, provides for consistency with the recitation of "resin" at line 3.

In claim 12, the change renders the claim consistent with what is recited in step c) of claim 1, which states "incubating".

In claim 14, the added text provides antecedent basis for "the second anion-exchanger flow-through in claim 15.

In claim 15, the added text provides antecedent basis for what is recited in further dependent claims 16-19.

In claims 16-19, "IgG" has been deleted at line 2, since it is redundant with "IgG" recited at line 1. The addition of "pH-adjusted second anion-exchanger flow-through" to



lines 2-3 makes it clear that the recited steps occur after the pH adjustment of claim 15. This sequence of steps is supported by Fig. 2 and by specification page 5, lines 18-28 and page 8, lines 20-34.

In claim 27, the addition of "adjusted to" is for clarity. The addition of "+/- 0.1" is supported by page 5, lines 18-19 and by page 8, lines 20-21 of the disclosure.

## CONTACTS

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, whose telephone number is 571-272-0849. The examiner can normally be reached on Mon.-Thu. from 8:00 am to 5:30 pm and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara, can be reached on 571-272-0878. The fax phone number for the organization where this application is assigned is 571-273-8300.

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Typed 2/25/09 DAS

/David A Saunders/

Primary Examiner, Art Unit 1644